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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,283	07/15/2005	Hans-Ulrich Petereit	273014US0PCT	5271

22850 7590 06/05/2009

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EXAMINER	
SASAN, ARADHANA	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
06/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/542,283	PETEREIT ET AL.	
	Examiner	Art Unit	
	ARADHANA SASAN	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 12-23* is/are pending in the application.

4a) Of the above claim(s) *1-4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 13-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The remarks and amendments filed on 03/11/09 are acknowledged.

2. Claims 1-4 were withdrawn. Claims 8-11 were cancelled. Claims 5, 13-14 and 23 were amended.

3. Claims 5-7 and 12-23 are included in the prosecution.

MAINTAINED REJECTIONS:

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 5-7, 12-15 and 18-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kajiyama et al. (US 5,545,492 B2).

The claimed invention is a powder with an average particle size of 200 μm or less, comprising (a) an anionic active pharmaceutical ingredient, (b) a copolymer which consists of free-radical polymerized C_1 to C_4 esters of acrylic or methacrylic acid and further (meth)acrylate monomers which have functional tertiary amino groups, and (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid, (d) with the proviso that less than 3% by weight based on the copolymer of an emulsifier having an HLB of at least 14 is present, wherein the powder when placed in the mouth immediately disintegrates and releases active ingredient (a). The powder is produced by vigorously

mixing (a) the anionic active pharmaceutical ingredient with (b) the copolymer consisting of free-radical polymerized C1 to C4 esters of acrylic or methacrylic acid and further (meth)acrylate monomers which have functional tertiary amino groups, and (c) 5 to 50% by weight, based on (b), of the C12 to C22 carboxylic acid in a melt, solidifying the mixture, grinding to an active ingredient-containing powder with an average particle size of 200 µm or less, and incorporating the powder into a water-soluble matrix of at least one pharmaceutically acceptable excipient.

Kajiyama teaches a quick disintegrating tablet in the buccal cavity comprising drug-containing particles with a mean particle diameter of approximately 50 ~ approximately 250µm, the drug-containing particles contain a bitter tasting drug and a pharmaceutical preparation carrier (Col. 1, lines 14-24). The "quick disintegrating tablet in buccal cavity" means "a tablet that is disintegrated in the buccal cavity within 1 minute by essentially saliva only without taking water for swallowing tablets" (Col. 5, lines 48-51). The bitter tasting drugs include ibuprofen (Col. 6, lines 38-42 and Col. 7, line 18). The pharmaceutical preparation carrier includes gastrosoluble acrylic polymers, such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer (for instance, brand name EUDRAGIT E, Rohm Co., Ltd.) (Col. 8, lines 11-26). Higher fatty acids such as stearic acid, lauric acid, myristic acid, and palmitic acid are disclosed (Col. 8, lines 38-41). Kajiyama teaches the advantages of the drug-containing particles as including alleviating the bitter taste of bitter tasting drugs and having the ability to quickly disintegrate and dissolve in the buccal cavity (Col. 6, lines 8-18).

Kajiyama does not expressly teach the weight percent of the carboxylic acid.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a quick disintegrating tablet with drug particles comprising a bitter tasting drug such as ibuprofen and gastrosoluble acrylic polymers (such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer) and higher fatty acids such as stearic acid, as taught by Kajiyama, modify the level of higher fatty acids such as stearic acid during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would do this because the level of higher fatty acids is a manipulatable parameter which can be modified during the process of routine experimentation.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 5, the active ingredient-containing powder with an average particle size of 200 μm or less would have been obvious over the drug-containing particles with a mean particle diameter of approximately 50 ~ approximately 250μm, as taught by Kajiyama (Col. 1, lines 14-24). The limitation of (a) an anionic active pharmaceutical ingredient would have been obvious over the ibuprofen taught by Kajiyama (Col. 6, lines 38-42 and Col. 7, line 18). The limitation of (b) a copolymer which consists of free-radical polymerized C_1 to C_4 esters of acrylic or methacrylic acid

and further (meth)acrylate monomers which have functional tertiary amino groups would have been obvious over the gastrosoluble acrylic polymers, such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer (for instance, brand name EUDRAGIT E, Rohm Co., Ltd.) taught by Kajiyama (Col. 8, lines 11-26). The limitation of (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid would have been obvious over the higher fatty acids such as stearic acid, lauric acid, myristic acid, and palmitic acid taught by Kajiyama (Col. 8, lines 38-41). One of ordinary skill in the art would modify the level of these fatty acids in the composition during the process of routine experimentation and the recited weight percent range would have been an obvious variant unless there is evidence of criticality or unexpected results. The proviso that less than 3% by weight based on the copolymer of an emulsifier having an HLB of at least 14 is present would have been obvious because "less than 3%" includes 0%, and there is no teaching of emulsifier or surfactant in the drug-containing particles taught by Kajiyama (Col. 1, lines 14-24). The limitation of the powder when placed in the mouth immediately disintegrates and releases active ingredient (a) would have been obvious over the "quick disintegrating tablet in buccal cavity" means "a tablet that is disintegrated in the buccal cavity within 1 minute by essentially saliva only without taking water for swallowing tablets" (Col. 5, lines 48-51).

Regarding instant claims 6-7, the limitation of the anionic analgesic and anionic antirheumatic would have been obvious over the ibuprofen, which is a known analgesic and antirheumatic, as taught by Kajiyama (Col. 7, line 18).

Regarding instant claims 12 and 13, the limitation of the anionic active pharmaceutical ingredient (a) that has been incorporated into the copolymer (b) would have been obvious over the particles containing a bitter tasting drug and a pharmaceutical preparation carrier (Col. 1, lines 14-24), where the pharmaceutical preparation carrier includes gastrosoluble acrylic polymers, such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer (for instance, brand name EUDRAGIT E, Rohm Co., Ltd.), as taught by Kajiyama (Col. 8, lines 11-26).

Regarding instant claim 14, the limitation of the carboxylic acid would have been obvious over the higher fatty acids such as stearic acid, lauric acid, myristic acid, and palmitic acid, as taught by Kajiyama (Col. 8, lines 38-41).

Regarding instant claim 15, the limitation of the powder that contains no emulsifier having an HLB of 14 or more would have been obvious because there is no teaching of emulsifier or surfactant in the drug-containing particles taught by Kajiyama (Col. 1, lines 14-24).

Regarding instant claim 18, the limitation of the bitterness value would have been obvious over the drug-containing particles that alleviate the bitter taste of bitter tasting drugs and quickly disintegrate and dissolve in the buccal cavity (within 1 minute), as taught by Kajiyama (Col. 6, lines 8-18, Col. 16, Table 1, and Col. 5, lines 48-51). One of ordinary skill in the art would determine the bitterness value using the standard methodology during the process of routine experimentation.

Regarding instant claims 19-20, the limitation of at least one pharmaceutically acceptable excipient would have been obvious over the lubricants such as magnesium stearate taught by Kajiyama (Col. 10, lines 12-13). One of ordinary skill in the art would use magnesium stearate because it is a commonly used lubricant in tablet formulations. The HLB of magnesium stearate is a property of the lubricant that is implicit with the inclusion of magnesium stearate in the composition. Please see MPEP 2112.01. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present.

Regarding instant claim 21, the limitation of a plasticizer would have been obvious over the plasticizers triacetin, triethyl citrate, and dibutyl sebacate as taught by Kajiyama (Col. 8, lines 48-51).

Regarding instant claim 22, the limitation of the form of the composition would have been obvious over the quick disintegrating tablet (Col. 1, lines 14-24) produced by molding under pressure to retain the tablet form (Col. 11, lines 3-6), as taught by Kajiyama.

Instant claim 23 is set forth in the form of a product-by-process claim, which is considered a product claim by the Office. Applicants are reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art. In *re Thorpe et al.* (CAFC 1985), supra; In *re Dike* (CCPA 1968) 394 F2d 584, 157 USPQ 581; Tri-Wall Containers, Inc. v. United States et al. (Ct Cls 1969) 408 F2d 748, 161 USPQ 116; In re Brown et al. (CCPA 1972) 450 F2d 531, 173 USPQ

685; Ex parte Edwards et al. (BPAI 1986) 231 USPQ 981. Instant claim 23 would have been obvious over the quick disintegrating tablet (Col. 1, lines 14-24) produced by molding under pressure to retain the tablet form (Col. 11, lines 3-6), as taught by Kajiyama.

6. Claims 16-17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kajiyama et al. (US 5,545,492 B2) in view of Smith et al. (US 6,194,000 B1).

The teaching of Kajiyama is stated above.

Kajiyama does not expressly teach a powder that contains an emulsifier having an HLB of at least 14.

Smith teaches immediate release particles of an NMDA receptor antagonist admixed with sodium lauryl sulfate (Col. 2, lines 2-3 and Col. 3, lines 29-36).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a quick disintegrating tablet with drug particles comprising a bitter tasting drug such as ibuprofen and gastrosoluble acrylic polymers (such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer) and higher fatty acids such as stearic acid, as taught by Kajiyama, combine it with the use of sodium lauryl sulfate in immediate release particles, as taught by Smith, and produce the instant invention.

One of ordinary skill in the art would do this because incorporating sodium lauryl sulfate into immediate release drug particles is known in the art, as evidenced by Smith.

Regarding instant claims 16-17, the limitations of 1-3% emulsifier having an HLB of 14 or more and the limitation of 1-2% emulsifier having an HLB of 14 or more would

have been obvious over the use of sodium lauryl sulfate (a known emulsifier) in immediate release particles, as taught by Smith (Col. 2, lines 2-3 and Col. 3, lines 29-36).

Response to Arguments

Claim Objections

7. In light of Applicants' amendment the objection to claim 13 is withdrawn.

Rejection of claims under 35 USC § 103(a)

8. Applicants' arguments, see Page 8, filed 03/11/09, with respect to the rejection of claims 5-7, 12-15 and 18-23 under 35 U.S.C. 103(a) as being unpatentable over Kajiyama et al. (US 5,545,492 B2) have been fully considered but are not persuasive.

Applicants argue that Kajiyama does not disclose or suggest the invention, because it is directed to a product produced by spray drying (see abstract, col. 10, lines 21 ff. and claims 1 and 13 of Kajiyama) and does not disclose or suggest the process steps now required by independent claim 5. Applicants argue that the process steps required by the invention provide a superior product, less likely to be contaminated or degraded, which differs from that of a spray dried powder, such as that of Kajiyama. Applicants argue that the spray drying method of Kajiyama has a lot of disadvantages that affect product quality and uniformity. Applicants argue that Kajiyama provides no guidance as to which combination of ingredients is useful in a melt process not involving water.

This is not persuasive because the amendment of claim 5 recites process steps. It is noted that the instant claims are set forth in the form of product-by-process claims,

which are considered product claims by the Office. Applicants are reminded that process limitations cannot impart patentability to a product that is not patentably distinguished over the prior art. In *re Thorpe et al.* (CAFC 1985), supra; In *re Dike* (CCPA 1968) 394 F2d 584, 157 USPQ 581; Tri-Wall Containers, Inc. v. United States et al. (Ct Cls 1969) 408 F2d 748, 161 USPQ 116; In re Brown et al. (CCPA 1972) 450 F2d 531, 173 USPQ 685; Ex parte Edwards et al. (BPAI 1986) 231 USPQ 981. Please see MPEP 2113.

The limitations of the product are rendered obvious by the teaching of Kajiyama (Col. 6, lines 38-42, Col. 7, line 18, Col. 8, lines 11-26, Col. 8, lines 38-41).

Applicants argue that Kajiyama provides no suggestion to combine the copolymers listed in col. 8 with higher fatty acids and that the Examples in Kajiyama also do not employ the combination required by the invention.

This is not persuasive because patents are relevant as prior art for all they contain and are not limited to the preferred embodiments or examples. Please see MPEP 2123. In this case Kajiyama teaches the gastrosoluble acrylic polymers, such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer (Col. 8, lines 11-26) and also teaches the higher fatty acids such as stearic acid, lauric acid, myristic acid, and palmitic acid (Col. 8, lines 38-41). One of ordinary skill in the art would find it obvious to combine the acrylic polymers with the higher fatty acids during the process of routine experimentation given that lubricants such as stearic acid are known in the art to be used in combination with active ingredients and polymers in compressed dosage forms to provide anti-adhesive properties.

Applicants argue that Kajiyama uses only cationic (famotidine, ambroxol) or neutral (acetaminophen) active pharmaceutical ingredients in its examples and that comparative examples 6 and 9 of the present application show that (both neutral) caffeine and paracetamol (=identical with acetaminophen) do not work.

This is not persuasive because Kajiyama teaches a quick disintegrating tablet containing a bitter tasting drug (Col. 1, lines 14-24) and further discloses ibuprofen as a bitter tasting drug (Col. 6, lines 38-42 and Col. 7, line 18). Therefore, the limitation of the (elected species) anionic active pharmaceutical ingredient is taught by Kajiyama. Please note that patents are relevant as prior art for all they contain and are not limited to the preferred embodiments or examples. Please see MPEP 2123.

Applicants argue that the superior bioavailability compared to the spray dried products such as those of Kajiyama results from the transfer of the active ingredient to a stadium of a solid solution during the melt process which produces the products of the invention.

This is not persuasive because Applicant has not provided comparative evidence to show that the product produced by a melt process is superior to products prepared by a spray drying process. The instant specification also does not provide comparisons between products produced by the two different processes. Moreover, instant claims are directed to a product and the limitations of the product are rendered obvious by the teachings of Kajiyama.

Therefore, the rejection of 12/11/08 is maintained.

9. Applicants' arguments, see Page 11, filed 03/11/09, with respect to the rejection of claims 16-17 under 35 U.S.C. 103(a) as being unpatentable over Kajiyama et al. (US 5,545,492 B2) in view of Smith et al. (US 6,194,000 B1)have been fully considered but are not persuasive.

Applicants argue that Smith was relied upon as a secondary reference teaching a powder containing an emulsifier having an HLB or at least 14 (*viz.* SDS), but does not disclose or suggest the elements of the invention absent from Kajiyama and that accordingly, this rejection may also be withdrawn.

This is not persuasive because Kajiyama does not teach a powder that contains an emulsifier having an HLB of at least 14 and Smith remedies this deficiency. All of the claimed elements are taught by Kajiyama and Smith and one with ordinary skill in the art could have combined the elements and the combination would have yielded predictable results. See *KSR International Co. v. Teleflex Inc.*, 550 U.S. - , 82 USPQ2d 1385 (2007).

Therefore, the rejection of 12/11/08 is maintained.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615